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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/458,779 12/10/99 LATTERICH

M 1211.001US1

021186 HM22/0705
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EXAMINER

DAVIS, K

ART UNIT

PAPER NUMBER

1636

DATE MAILED:

07/05/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/458,779

Applicant(s)

LATTERICH ET AL.

Examiner

Katharine F. Davis

Art Unit

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 April 2001.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 3-12, 14-23, 25-27, 29-34 & 36-46 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 3-12, 14-23, 25-27, 29-34 & 36-46 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 12.
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

DETAILED ACTION

This Office Action is in response to the Amendment filed April 18, 2001. Claims 1, 2, 13, 24, 28 and 35 have been canceled. New claims 43-46 have been added. Claims 3-12, 14-23, 25-27, 29-34 and 36-46 are pending in the instant application.

The rejections of claims 1, 2, 13, 24, 28 and 35 under 35 U.S.C. 112, first and second paragraphs have been withdrawn in view of the cancellation of the claims. The rejections of claims 1-42 under 35 U.S.C. 112, second paragraph have been withdrawn in view of the amendments to the claims and the remarks presented by the applicants in the April 18, 2001 Response.

Claim Objections

Claim 12 is objected to because of the following informality: it is dependent from a canceled base claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Art Unit: 1636

Claims 3-12, 14-23, 25-27, 29-34, 36-42 and 44-46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is based on the Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, first paragraph "Written Description" Requirement published in the Federal Register (Volume 64, Number 244, Pages 71427-71440). Claims 3-12, 14-23, 25-27, 29-34, 36-42 and 44-46 are drawn to a polynucleotide comprising a sequence encoding a functional vesicular fusion factor 2 protein (Vff2p) comprising SEQ ID NO:2 or a variant of Vff2 protein, vectors for expression of said polynucleotide, the Vff2 protein encoded by said polynucleotide, and methods for using said polynucleotide and protein to increase protein production and secretion in a cell. The instant specification defines a "variant" of Vff2 to be a polypeptide that is not completely identical to the native Vff2 protein. These are genus claims encompassing any protein and/or nucleic acid sequence from any organism that is not completely identical to the Vff2 protein comprising SEQ ID NO:2. The present specification discloses the nucleic acid sequence and the protein sequence of Vff2 from the yeast *Saccharomyces cerevisiae*. The specification teaches that a variant of the Vff2 protein may be obtained by altering the amino acid sequence by insertion, deletion or substitution of one or more amino acids however it does not teach what amino acids are altered. Thus, the term "variant" does not have specific limitations. The disclosure of Vff2 from the yeast *Saccharomyces cerevisiae* is not deemed to be descriptive of the complete structure of a representative number of species (variants of Vff2) encompassed by the claims as one of skill in the art cannot envision the

Art Unit: 1636

complete sequence of any other variant protein and/or nucleic acid based on the disclosed protein and nucleic acid sequence. Additionally, there is no description of a representative number of species by partial structure and a function which correlates with structure as there is no disclosure of the specific protein and/or nucleic acid sequences necessary for activity of Vff2p in the cellular secretory pathway. According to the teachings of the instant specification the yeast Vff2 protein is involved in the secretory pathway and/or involved in membrane fusion however there is no teaching of what domains and/or motifs are responsible for these functions of the Vff2 protein. Thus, a skilled artisan would be uncertain as to which protein domains to target in order to obtain Vff2 variant proteins. Therefore, the specification does not describe the claimed protein and nucleic acid sequences in such full, clear, concise and exact terms so as to indicate that the applicants had possession of these sequences (other than SEQ ID NOs:1 and 2) at the time of filing of the present application. Thus, the written description requirement has not been satisfied.

Claims 3-12, 14-23, 25-27, 29-34, 36-42 and 44-46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide with a sequence of SEQ ID NO:1, a protein with a sequence of SEQ ID NO:2, and a host cell (*Saccharomyces cerevisiae*), does not reasonably provide enablement for polynucleotide and/or protein variants other than SEQ ID NOs:1 and 2 or a host cell other than *Saccharomyces cerevisiae*. The specification does not enable any person skilled in the art to which it pertains, or with which it is

Art Unit: 1636

most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The following factors have been considered in formulating this rejection (*In re Wands*, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

The instant claims are broad in that they encompass both the Vff2 protein from *Saccharomyces cerevisiae* and any protein and/or nucleic acid sequence from any other organism or altered version of the *Saccharomyces cerevisiae* sequence that is not completely identical to the native Vff2 protein.

The nature of the invention is a method of using a protein (Vff2) to increase intracellular production and/or secretion of a target heterologous protein in a cellular expression system.

An analysis of the prior art indicates that at the time that the instant invention was made one of skill in the art did not know how to make and/or use a Vff2 protein.

The skill of those in the art of recombinant engineering and protein expression in yeast is high.

The area of the invention is unpredictable. As indicated above, one of skill in the art could not predictably carry out the invention in its full scope based on knowledge in the prior art. While one of skill in the art may agree that the percent identity of sequences from other species that may be homologous to Vff2 is in fact high (page 11 of the specification), homology by sequence alone does not predict function. The skilled artisan would not be able to identify the

Art Unit: 1636

bases and/or residues that can be changed while still maintaining a functional protein. Applicants provide no evidence that these potential homologs exhibit a similar function to that of the Vff2 protein.

The instant specification provides little direction or guidance to support the claimed invention in its full scope. A general teaching on amino acid substitutions, deletions and/or insertions is not considered to be sufficient guidance to enable every possible variant of Vff2 protein. The instant specification is silent considering what domains and/or motifs are responsible for the function of the Vff2 protein. Thus, a skilled artisan would be uncertain as to which protein domains to target in order to obtain Vff2 variant proteins.

The working examples relate only to Vff2 protein as SEQ ID NOs: 1 and 2 wherein the host cell is *Saccharomyces cerevisiae*.

The quantity of experimentation necessary to carry out the claimed invention is high as the skilled artisan could not rely on the prior art or the instant specification to teach how to make or use any variant of the Vff2 protein. In order to make the claimed variants of Vff2 one of skill in the art would have to identify those mutations that do not destroy the function of the Vff2 protein. This identification would involve screening a large number of Vff2 sequences without any guidance as to where to begin screening which constitutes undue experimentation.

Applicants' arguments presented on pages 10 and 11 of the Response filed April 18, 2001 have been carefully considered but are not found to be convincing. Monoclonal antibody technology is a well-developed field wherein it is standard practice to screen hybridomas to identify a desirable monoclonal antibody and one of skill in this art knows that the desired antibody could be

Art Unit: 1636

obtained with sufficient screening. The field of the instant invention is not as well-developed a field consequently there is not the same high expectation of success.

Based on the broad scope of the claims, the nature of the invention, the skill of those in the art, the unpredictability of the area of the invention, the lack of sufficient guidance or working examples in the specification and the quantity of experimentation necessary, it would clearly require undue experimentation by one of skill in the art to make and use any variant of the Vff2 protein.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 31-34 and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 31 is incomplete. There is no positive process step(s) which refers back to the method recited in the preamble therefore rendering the claim indefinite.

Claims 31 and 33 recite the phrase "...has at least 40% homology to SEQ ID NO:2". There are many definitions in the art as to what is considered to be homologous. Therefore, the metes and bounds of the claims are undetermined thus rendering the claims indefinite.

Claims 32 and 34 recite the term "the encoded Vff2p". There is insufficient antecedent basis for this term in the claims.

Art Unit: 1636

Claim 44 is indefinite because it refers to the protein of claim 25 however claim 25 refers to a recombinant host cell.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 3-12, 14-23, 25-27, 29-34 and 36-46 are rejected under 35 U.S.C. 102(a) as being anticipated by Powell *et al.* (Mol. Biol. Cell 10(Suppl):298a, abstract No. 1727, November 1999, IDS reference). Powell *et al.* disclose a 32 kilodalton vesicle fusion factor 2 (Vff2) protein that is involved in membrane fusion. In the absence of evidence to the contrary, this protein appears to be the same protein or a variant thereof that is claimed in the instant invention.


Conclusion

Claims 3-12, 14-23, 25-27, 29-34 and 36-46 are rejected. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Katharine F. Davis whose telephone number is (703) 605-1195 with direct desktop RightFax (703)746-5199.

Art Unit: 1636

The examiner can normally be reached on Monday-Friday (8:30am-5:00pm). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Schwartzman can be reached on (703) 308-7307. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-1935 for After Final communications. Any inquiry concerning the formalities of this application should be directed to Patent Analyst Dianiece Jacobs whose telephone number is (703) 305-3388. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Katharine F. Davis
July 2, 2001


ROBERT A. SCHWARTZMAN
PRIMARY EXAMINER